

**MASSACHUSETTS DEPARTMENT OF PUBLIC HEALTH
BUREAU OF COMMUNICABLE DISEASE CONTROL
DIVISION OF EPIDEMIOLOGY AND IMMUNIZATION
(617) 983-6800**

PREVENTION OF RABIES IN HUMANS

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CONTENTS

I. Summary of recent information	p.1
II. Evaluating exposures to animals	p.2
III. Post-exposure prophylaxis	p.6
IV. Pre-exposure prophylaxis	p. 9
V. Prevention of rabies	p.9
VI. References	p. 10

APPENDICES

Appendix 1: Guide to rabies evaluation and management	p.11
Appendix 2: Algorithm: Management of human exposures to suspect rabid animals	p.12
Appendix 3: Recommendations for Post-exposure prophylaxis	p.14
Appendix 4: Recommendations for Pre-exposure prophylaxis	p.15
Appendix 5: Rabies-human disease	p.16
Appendix 6: Epidemiology of rabies in humans	p.18
Appendix 7: Post-exposure prophylaxis reporting form	p.19
Appendix 8: Useful rabies contact information	p.20

1. SUMMARY OF RECENT INFORMATION REGARDING RABIES

This section offers a brief description of recent developments in epidemiology, policy, and pharmaceuticals. Some of the information presented here is repeated in later sections that provide more detail on the particular subjects.

A. MANAGING EXPOSURES OR POTENTIAL EXPOSURES TO BATS

Bat strain rabies has been documented in Massachusetts since 1961, and infected bats have been identified throughout the state. Since 1990, 92% of the 26 domestically-acquired rabies cases in humans in the United States have involved bat strain rabies. Of those infected with bat strain rabies, a history of exposure to a bat was not documented in 88% of the cases. This finding suggests that even limited contact with bats may be associated with transmission. Bat bites may be less severe, and therefore more difficult to recognize than bites from larger animals. Post-exposure prophylaxis should be given in any situation where a bat is physically present and a bite, or any other exposure/contact, cannot be ruled out. In situations in which there is reasonable probability that such contact occurred (e.g. a sleeping

individual awakes to find a bat in the room, an adult witnesses a bat in the room with a previously unattended child, mentally challenged person, intoxicated individual, etc.), post-exposure prophylaxis is appropriate even in the absence of a demonstrable bite or scratch. If the bat is available and can be tested promptly, post-exposure prophylaxis may be postponed pending results. It is also important to inform first-responders that bats captured following a human exposure should NEVER be released.

B. RABID CATS AND DOGS

Since the raccoon rabies outbreak entered the state in 1992, more than 90 cats have tested positive for rabies. Of these more than three-fourths were strays or recently acquired strays. People should be discouraged from approaching unfamiliar cats and dogs because of the risk of exposure to rabies. Physicians should consider exposures to strays as high risk for rabies. In 2001, Massachusetts had a dog test positive for rabies; it was a recently acquired pet that was too young to have been completely vaccinated. The total numbers of dogs and cats that have tested positive for rabies in Massachusetts since 1992 are 4 and 92, respectively.

C. PERSISTENCE OF RACCOON RABIES EPIDEMIC

Raccoon rabies has spread to approximately 90% of cities and towns in Massachusetts and has become endemic except on Cape Cod and the islands of Martha's Vineyard and Nantucket. The message for residents is clear: raccoon rabies has not gone away, and people should continue to take precautions to protect themselves and their pets. Physicians should also realize that the persistence of raccoon rabies means that all human exposures to high-risk animals should be evaluated carefully.

D. VACCINES FOR HUMAN PRE AND POST EXPOSURE PROPHYLAXIS

The intradermal (ID) form of the Human Diploid Cell Vaccine (HDCV) for pre-exposure prophylaxis is no longer available. Pre-exposure prophylaxis now requires a three-dose intramuscular (IM) series.

II. EVALUATING EXPOSURES TO WILD AND DOMESTIC ANIMALS

The principal risk of exposure of humans to rabies arises from contact with unvaccinated domestic animals, which serve as a bridge from wildlife to humans. Many other exposures occur through feeding, petting, caring for, or having other contact with wild animals, including bats.

Since rabies post-exposure prophylaxis is costly, can be painful, and is sometimes associated with mild local and systemic side effects, it should not be administered indiscriminately. Decisions to give post-exposure prophylaxis after a human has been exposed to a potentially rabid animal should be based on the following: (1) the type of animal, i.e., whether it is a high-risk or low-risk animal, (2) the health of the animal, i.e., whether it is exhibiting signs consistent with rabies, (3) the availability of the exposing animal for testing or, if it is a domestic animal (dog, cat, ferret) or livestock (cattle, horse, sheep), for quarantine, (4) whether the bite was provoked or unprovoked, (5) type of exposure, and (6) knowledge of the epidemiology of rabies in the area. Now that raccoon and bat rabies are found throughout Massachusetts, all of Massachusetts is considered endemic for animal rabies, and exposures should be evaluated with this in mind.

The Division of Epidemiology and Immunization at the Massachusetts Department of Public Health (MDPH) is available for consultation about exposures:

Weekdays – (617) 983-6800

Evenings/weekends (emergencies) – (617) 983-6200

A. RISKS OF RABIES ASSOCIATED WITH DIFFERENT ANIMALS

1. domestic animals and livestock

Domestic animals and livestock are of significant concern because they can serve as the bridge between rabies in wild animals and humans. Since raccoon rabies entered Massachusetts in 1992, 4 dogs, 92 cats, 11 cattle and 3 horses have tested positive for rabies in the state. After a domestic animal (dog, cat or ferret) or a livestock (cattle, horse, or sheep) bites or scratches a person, these animals (for which there is a USDA-approved rabies vaccine), regardless of their vaccination status, should be quarantined for ten days if they are healthy and available. Rabies vaccinations in domestic animals and livestock are not 100% effective, and rare cases of vaccinated domestic animals and livestock developing rabies have occurred, so these animals need to be quarantined just like unvaccinated ones. If the animal is healthy at the end of the ten-day quarantine period, post-exposure prophylaxis is not recommended. If the animal exhibits signs of rabies or dies within the ten-day quarantine period, it may be necessary to initiate post-exposure prophylaxis (see Appendix 1).

2. bats

Bats are considered high risk for rabies. Exposures or potential exposures to bats should be carefully evaluated. Because the size of bites or scratches from bats may be very small, individuals may not recognize that an exposure has occurred. Thus, bat bites may go unnoticed or be mistaken for an insect bite or sting. Post-exposure prophylaxis should be given in any situation in which a bat is physically present and a bite, or any other exposure or contact, cannot be ruled out. In situations in which there is reasonable probability that such contact occurred (e.g. a sleeping individual awakes to find a bat in the room, an adult witnesses a bat in the room with a previously unattended child, mentally challenged person, intoxicated individual, etc.), post-exposure prophylaxis is appropriate, even in the absence of a demonstrable bite or scratch. If the bat is available and can be tested promptly, prophylaxis may be postponed pending test results.

3. high-risk wild animals

Wild animals considered to be high risk for acquiring rabies include: raccoons, bats, skunks, foxes, woodchucks, and coyotes. If a person is bitten or otherwise exposed (refer to section B2 for exposure definition) to one of these animals, the animal should be tested for rabies as soon as possible. If the animal is positive for rabies, the individual should begin post-exposure prophylaxis. If the animal tests negative, post-exposure prophylaxis is not recommended. Although post-exposure prophylaxis should begin as soon as possible after exposure, it is reasonable to wait for test results before beginning. If there are questions regarding a delay in testing, call the MDPH for advice (617) 983-6800. If the exposing animal is not available for testing, it should be assumed to be rabid, and post-exposure prophylaxis decisions should be made accordingly.

4. small wild mammals

Wild rodents, insectivores (shrews and moles) and lagomorphs (rabbits and hares) are very low risk animals for rabies. When people are bitten by these animals, prophylaxis is rarely required, and testing of the animal for rabies is rarely recommended. These animals are so small that if a rabid animal (raccoon, skunk, fox, etc.) were to attack, the animal would likely die before having a chance to develop rabies. They may also be less susceptible to infection with the rabies virus, or may seek and remain in shelter after resisting attack or becoming ill with rabies. Only when

such animals attack in an unprovoked manner should there be suspicion of rabies. Small animals, such as squirrels and chipmunks that bite humans who are feeding them, are acting normally. Such bites are considered provoked, and people should be taught not to hand feed wild animals. Squirrels are unlikely to present with rabies, and their bites almost never require prophylaxis.

The only exceptions to this list of animals are woodchucks, (refer to #3, above) also called groundhogs, which are considered at high risk for acquiring rabies. Other larger aquatic mammals, such as beavers, muskrats, and otters, which are considered at intermediate risk for rabies, may be large enough to fight off an attack by a rabid animal, and they may have the opportunity to infect other animals and humans.

5. rodents and other small mammals caged outdoors

Outdoor cages housing rodents and lagomorphs may allow exposure to rabid animals, but offer enough protection so that these smaller animals survive the exposure. There have been rabies cases reported in animals caged outdoors in this manner. If a small animal caged outdoors exposes a human and is not available for testing, post-exposure prophylaxis is recommended.

6. rodents and other small mammals caged indoors

Some small mammals such as hamsters, gerbils, rats, mice, and rabbits are caged exclusively indoors. If these animals have been caged exclusively indoors for the past six months, treatment would not be recommended for a person bitten or otherwise exposed to them.

B. EVALUATING RISK OF EXPOSURE

1. type of exposure

The risk of rabies to an exposed individual varies depending on the type of exposure. The risk of rabies after a bite by a rabid animal (5-80%) is about 50 times the risk after scratches (0.1-1.0%). The risk of rabies after contamination of minor wounds with infected saliva is very low (<0.1%). The risk after bites depends on the severity of the bite (>80% after multiple bites by rabid wolves) and the site of exposure. The risk of rabies after bites on lower extremities (5%) or bites on upper extremities (25%) is markedly less than the risk after a bite to the head (60%). All of these risk estimates are in the absence of post-exposure prophylaxis and are largely based on nineteenth century historical records.

Although rare, four cases of human rabies have been attributed to airborne exposures: two in laboratories and two in caves heavily infested with bats. Airborne exposure is not considered risky except in specialized circumstances, for instance, when a person spends time in a confined space with high concentrations of rabies virus, such as in bat caves or laboratories where rabies virus is present. Pre-exposure immunization is recommended for spelunkers and persons working with rabies virus in a laboratory.

2. category of exposure

There are two categories of direct (primary) exposure: bite and non-bite. Non-bite exposures include scratches, abrasions, and open wounds or mucous membranes contaminated with saliva or other potentially infectious material, such as brain tissue. If the material is dry, it can be considered non-infectious; sunlight, ultraviolet (UV) light, and detergent inactivate the virus. Evaluation of indirect (secondary) exposures can be more difficult than the evaluation of direct

exposures. Indirect exposures to rabies can occur when saliva, or other infectious material (i.e. nervous tissue) from a rabid animal enters a fresh cut (cut wound that has been bleeding in the past 24 hours) or scratch or a mucous membrane (eye, nose, or mouth). For example, people handling a dog or cat within a short time after it has encountered a rabid animal may have been indirectly exposed to rabies, particularly if saliva from the rabid animal was on the dog or cat's fur. Although there has never been a documented case of human rabies resulting from a secondary exposure, the factors that should be considered include the time since the pet's exposure to the potentially rabid animal, the ambient weather conditions (temperature and humidity), and whether the contact of the domestic animal with the human involved an open wound (bleeding within the prior 24 hours) or mucous membranes. The rabies virus is fragile. Under ideal laboratory conditions, it can survive for 24 hours at 40° F and for 4 hours at 104° F. However, common environments do not provide ideal conditions and survival time in the natural environment is variable, but short.

3. situations with little or no risk

Petting a rabid animal or coming into contact with an animal's blood, urine, feces, or skunk spray does **NOT** constitute an exposure or require prophylaxis, unless the animal is a bat. However, if these body parts/secretions are mixed with saliva, the exposure should be evaluated accordingly.

C. BEHAVIOR OF ANIMALS WITH RABIES

Animals with rabies can appear aggressive ("furious rabies") or normal or meek ("dumb rabies"). Common signs of rabies include neurologic signs, such as paralysis and ataxia, and hypersalivation. Rabies virus can be shed in saliva for days before signs of rabies appear. Therefore, the behavior of the animal, is **NOT** a reliable indicator of whether or not the human exposed, is at risk.

D. REPORTING EXPOSURES

In order to facilitate animal control efforts (quarantine, euthanasia, etc.), all animal bites should be reported as follows:

- Report animal bites to humans to the local board of health or other designated local officials.
- Also report animal bites or other exposures to the appropriate agencies as follows:
 1. For human exposures to domestic animals other than ferrets: Bureau of Animal Health, Department of Food and Agriculture (617- 626-1794).
 2. For human exposures to ferrets: Division of Fisheries and Wildlife, Department of Fisheries, Wildlife and Environmental Law Enforcement (617-727-3151).

E. ADDITIONAL GUIDELINES

Guidelines for decision making about post exposure prophylaxis can be found in Appendix 1. Additional guidance about information gathering and decision making after human exposures can be found in Appendix 2, the algorithm: "Management of Human Exposures to Suspect Rabid Animals."

III. POST-EXPOSURE PROPHYLAXIS

A. REPORTING

Effective July 29, 1995, the initiation of rabies post-exposure prophylaxis became reportable directly to the MDPH (105 CMR 300.140). In the City of Boston, providers are requested to report to the Boston Public Health Commission. Appropriate reporting forms can be obtained from your local board of health or from the Division of Epidemiology and Immunization at (617) 983-6800. A copy of this form is also attached in Appendix 7.

B. RABIES LOCAL WOUND MANAGEMENT

Local wound management following an animal bite consists of vigorous washing with soap and water for 10 minutes and a Td booster if more than 5 years have been elapsed since the last dose of tetanus vaccine. The decision to suture must be evaluated by weighing cosmetic factors against the risk of bacterial infection. Prophylactic antibiotics should be administered as indicated.

C. RABIES VACCINE

All rabies vaccines used in the United States are killed, cell culture-derived vaccines. Human Diploid Cell Vaccine (HDCV), grown in human fibroblasts, is inactivated with beta-propiolactone and ultra-filtration and contains neomycin. It is effective if given with HRIG promptly following exposure. The dose is 1cc (2.5 IU) IM, regardless of age and weight. Adults and children should receive HDCV in the deltoid area and infants in the antero-lateral thigh. HDCV is manufactured and distributed by Aventis-Pasteur (1-800-VACCINE).

Rabies Vaccine Adsorbed (RVA) is another vaccine licensed in the U.S. It is manufactured and distributed by BioPort Corporation. **At the present time, BioPort is not manufacturing or distributing RVA.** RVA is produced from virus grown in fetal rhesus lung diploid cells concentrated by absorption or aluminum phosphate. RVA is administered IM as described for HDCV. To contact BioPort for general information about the future availability of vaccine, or technical questions, call (517) 327-1500.

A purified chick embryo cell (PCEC) vaccine is another vaccine licensed in the U.S. It became available in the U.S. in the fall of 1997. It is manufactured and distributed by Chiron Corporation. It is prepared from the fixed rabies virus strain Flury LEP grown in primary cultures of chicken fibroblasts. The virus is inactivated with beta-propiolactone and further processed by zonal centrifugation in a sucrose density gradient. It is formulated for IM administration only. PCEC is available in a single-dose vial containing lyophilized vaccine that is reconstituted in the vial with the accompanying diluent, to a final volume of 1.0 ml just before administration. Contact Chiron at 1-800-CHIRON-8.

1. administration

The correct post-exposure prophylaxis schedule depends on whether or not the individual has ever previously received complete pre-exposure or post-exposure vaccination. The two recommended schedules can be found in Appendix 3.

Once it has been determined that an exposure has occurred, the administration of post-exposure prophylaxis in previously unvaccinated people must include, both human rabies immune globulin (HRIG) and either HDCV, RVA or PCEC. In persons with previous complete pre-exposure or

post-exposure prophylaxis received in the U.S. since 1980, post-exposure prophylaxis involves the administration of two doses of vaccine without human rabies immune globulin. In persons with a previous incomplete series of pre-exposure prophylaxis or post-exposure prophylaxis, a titer should be drawn to determine the immune response level before determining the post-exposure prophylaxis schedule. If a titer is not obtained, treatment should be initiated as if the individual was considered not previously vaccinated.

2. reactions

HDCV is a safe vaccine. Local reactions are reported in 25% of recipients, and mild systemic reactions occur in 20% of recipients. Immune complex-like and allergic reactions may occur in up to 6% of recipients beginning on average 21 days post-dose. These reactions are thought to be due to modification of human serum albumin (used as a stabilizer) by beta-propiolactone. Three cases of neurologic illness resembling Guillain-Barré syndrome have been reported, and all three resolved without sequelae. Local and mild systemic reactions after vaccination with RVA and PCEC appear similar in nature and frequency to those observed with HDCV. There are no contraindications to the use of HDCV, RVA or PCEC when there is an indication for post-exposure prophylaxis. No fetal abnormalities have been associated with HDCV, RVA or PCEC, so post-exposure prophylaxis should be administered to pregnant women, if indicated. Decisions about pre-exposure immunization should be made on a case by case basis.

3. efficacy

According to a CDC study, 100% of persons demonstrated antibody titers 2 to 4 weeks after completion of pre-or post-exposure immunization with licensed rabies vaccine.

No post-exposure vaccine failures have been reported in the U.S., in persons who have had post-exposure prophylaxis initiated before symptom onset. Failures in other countries have been associated with deviation from the prescribed schedule for post-exposure prophylaxis.

Vaccine failure has been associated with administration of vaccine in the gluteus. If one to two doses of vaccine have been given in the gluteus, repeat the doses in the deltoid muscles and readjust the schedule so four IM doses are administered in the deltoid muscles during the first 14 days. If three doses have been given in the gluteus, check antibody titers and readjust the schedule per CDC and the manufacturer's recommendations.

Failure to give HRIG correctly has also been associated with vaccine failure. Do not give more than the recommended dose, and do not give HRIG at more than 7 days post-initiation of vaccine. Vaccine failure is also associated with immunosuppression due to underlying illness or treatment, including treatment for the prevention of malaria. For immunosuppressed individuals, check antibody titers and adjust the schedule accordingly. Finally, in other countries, vaccine failure has been associated with lack of local wound cleaning. Although this problem has not been experienced in the U.S., thorough wound cleaning is highly recommended.

4. serologic testing

Serologic testing after post-exposure prophylaxis is not indicated if using HDCV, RVA or PCEC, if these vaccines are administered correctly, and if the individual is not immunocompromised.

If serologic testing is indicated after post-exposure prophylaxis, the standard test for evaluation is the rapid fluorescent focus inhibition test (RFFIT). This test is performed on human specimens at the following laboratories: Atlanta Health Associates, Inc. (telephone: 800-717-5612), the NE Georgia Reference Laboratory (telephone: 706-613-0077) and the Maryland State Rabies Lab (telephone: 410-767-6176). Call these laboratories for information on appropriate specimens to submit and packing and shipping recommendations. If titers are obtained, specimens collected 2-4 weeks after pre-exposure or post-exposure prophylaxis should completely neutralize challenge virus at a 1:25 serum dilution by RFFIT (or 0.5 IU recommended by WHO).

5. “off-schedule” post- exposure prophylaxis:

During the first two weeks of the schedule, if an individual misses any of the doses, adjust the schedule so that they receive four doses during the first 14 days post exposure. The fifth dose can be given at 28 days post exposure.

If an individual misses any of the doses during the second two weeks of the schedule, consult the manufacturer and adjust the schedule accordingly. An individual must receive at least five doses in total. The fifth doses can be given at 28 or more days following the initiation of post-exposure prophylaxis.

D. HUMAN RABIES IMMUNE GLOBULIN

Immune serum has been used to treat potential exposures to rabies for the past century. When given with rabies vaccine it is more effective than vaccine alone. When injected around the site of exposure, immune serum neutralizes virus and prevents invasion of the peripheral nervous system. Human rabies immune globulin (HRIG) produced by Aventis-Pasteur, inc. is distributed as “Imogam”. “Imogam” is available by calling 1-800-VACCINE.

1. administration

Always draw up HRIG in a separate syringe from vaccine. To administer HRIG, infiltrate as much of it as possible around, but not into, the wound(s). Give the remainder at an intramuscular site (usually the gluteus) different from that used for the vaccine.

The dose of HRIG is 20 IU/kg, and each cc of HRIG contains 150 IU. HRIG is supplied in two forms, a 2 cc (pediatric) vial and a 10cc (adult) vial. The average adult dose is 1400 IU, or 9cc. HRIG is effective if given promptly following an exposure by a rabid or potentially rabid animal. Do not give HRIG if more than 7 days have elapsed after initiation of vaccine, and do not increase or repeat the dose of HRIG. Doing so will interfere with antibody response to vaccine. Refer to Appendix 1, for timing of post-exposure prophylaxis in relation to exposure for quarantine, testing, and unavailable animals.

2. reactions

Human Rabies Immune Globulin (HRIG), licensed in the U.S. in 1975, is very safe. Reactions, such as local tenderness, soreness, and stiffness, are rare. Urticaria and other mild systemic reactions, such as mild fever and muscle aches, are also very rare.

3. Administration of live viral vaccines after HRIG

Do not give live viral vaccines for four months after giving HRIG.

E. ADDITIONAL GUIDELINES

Guidelines for administering post-exposure prophylaxis can be found in Appendix 3.

IV. PRE EXPOSURE PROPHYLAXIS

Pre-exposure vaccination is important in protecting those at high risk of exposure to rabid animals or rabies virus, such as veterinarians, animal handlers, certain laboratory workers and others whose activities put them at high risk of apparent, or more importantly, inapparent exposure. Pre-exposure vaccination is also important for travelers who will be spending more than one month in countries where canine rabies is endemic and post-exposure prophylaxis may be delayed or immunizing products may be unsafe or not available.

ACIP recommendations for pre-exposure prophylaxis by risk category/occupation and the local epidemiology of rabies can be found in Appendix 4. The attachment also includes recommendations for serologic testing, the need for booster doses and the recommended pre-exposure schedules for the vaccine formulations available in the U.S.

Please note, “Imovax Rabies” vaccine (Aventis-Pasteur) , RVA (BioPort), and “RabAvert” vaccine (Chiron Corporation) are licensed for intramuscular administration only. “Imovax Rabies” cannot be given intradermally. The only formulation which was given intradermally is “Imovax Rabies I.D.” (Aventis-Pasteur), however this formulation is no longer available.

V. PREVENTION OF RABIES

Massachusetts data show that most post-exposure prophylaxis is given following direct exposures to domestic animals (bites, scratches). Post-exposure prophylaxis in most of these situations is preventable, either through personal protective measures (not petting or feeding unfamiliar dogs and cats) or through quarantining animals that have exposed persons. Some persons with indirect exposures are treated because they handle dogs and cats that have recently fought with rabid wild animals. Avoiding close contact with dogs and cats in these circumstances, or wearing gloves to clean their wounds, prevents these indirect exposures.

Health care providers are encouraged to gather information on household pets and their vaccination status during routine health care visits and to provide prevention guidelines such as those presented in the following table.

For a detailed explanation of human rabies see Appendix 5. Appendix 6 provides information on the epidemiology of human cases in the U.S. since 1981.

PUBLIC EDUCATION GUIDELINES TO REDUCE RABIES EXPOSURES

- Vaccinate all pet cats, dogs, and ferrets against rabies.
- Do not touch, pick up, or feed wild or stray animals of any kind.
- Teach children to avoid wildlife and strays.
- Avoid sick or strangely acting animals.
- Fasten trash can lids tightly. Garbage attracts raccoons and skunks.
- Cap chimneys and seal openings into houses, etc., to prevent raccoons from entering or building dens.
- If you are bitten or scratched by any animal, you should wash the wound(s) promptly with warm soapy water and contact a doctor immediately.
- If your pet has been bitten or scratched by any animal, **wear gloves**, wash the wound with warm soapy water for at least ten minutes, and contact your veterinarian immediately.

VI. REFERENCES

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If you have suggestions about making this document more user-friendly for future editions, please send us your suggestions by mail (Epidemiology Program, MDPH, 305 South Street, Jamaica Plain, MA 02130), by fax (617-983-6840), or by phone (617-983-6800).

APPENDIX 1: GUIDE TO RABIES POST-EXPOSURE EVALUATION AND MANAGEMENT

Animal type	Evaluation and disposition of animal	Post-exposure prophylaxis (PEP) recommendation
Dogs, cats, ferrets, cattle, horses and sheep	<u>Healthy</u> and available for 10 days observation, quarantine regardless of vaccination status.	Should not begin PEP unless animals develops rabies
	Rabid	Immediate PEP
	Suspected Rabid Available for testing	Await testing results; begin PEP immediately if the animal is positive for rabies.
	Unavailable for testing	Immediate PEP
	Unknown (escaped)	Immediate PEP
Skunks, raccoons, bats, ² foxes, and most other carnivores, including dog/wolf hybrids ³ ; woodchucks and livestock for which there is NO USDA-approved rabies vaccine	Regard as rabid until animal proven negative by laboratory tests. ⁴ (Animal available for testing.)	Await testing results; begin PEP immediately if the animal is positive for rabies.
	Animal unavailable for testing	Immediate PEP
Rodents (except woodchucks), and lagomorphs (rabbits and hares) and other small mammals except bats	Consider individually	Bites of squirrels, hamsters, guinea pigs, gerbils, chipmunks, rats, mice, other small rodents, rabbits, and hares almost never require PEP. However, testing and/or PEP is indicated in some circumstances.

- 1 If a dog, cat, ferret, cattle, horse or sheep being held for the 10-day quarantine develops signs of rabies or signs of any illness, it should be euthanized and tested immediately. If the results are positive, the exposed person should begin PEP immediately.
- 2 Since the size of bites or scratches by bats may be very small, individuals may fail to recognize that an exposure has occurred. Thus, bat bites may go unnoticed or be mistaken for an insect bite or sting. **Post-exposure treatment** should be **given** in any situation where a bat is physically present and a **bite**, or any **other exposure/contact, cannot be ruled out**. This is particularly important when children are involved, and there are no witnesses to rule out a potential exposure.
- 3 Dog/wolf hybrids, regardless of vaccination history, should be considered as wild, unvaccinated animals.
- 4 The animal should be killed and tested as soon as possible. Holding for observation is not recommended. Do not give post-exposure prophylaxis if immunofluorescence test results of the animal are negative.
- 5 Rodents (except woodchucks), lagomorphs (rabbits, hare), and other small mammals except bats:
 - a) **Small mammals caged outdoors:** Outdoor cages may allow exposure to rabid animals, and several rabies cases have been reported from animals caged in this manner. If the animal is not available for testing, post-exposure prophylaxis is recommended.
 - b) **Small mammals caged indoors:** Healthy hamsters, gerbils, rats, mice, and rabbits, etc. which have been caged **exclusively indoors** for the past 6 months and which have no history of receiving a modified live rabies vaccine, pose no risk. Treatment would not be recommended for the exposed person.
 - c) **Wild rodents, lagomorphs and other small mammals except bats:** These animals are unlikely to have rabies. Each exposure needs to be evaluated as outlined below.
 - i) **Provoked bite:** If the bite was provoked (such as through feeding, petting, or playing with the animal) and the animal appeared healthy, it is unlikely that the animal was rabid at the time of the bite and most experts would not recommend post-exposure prophylaxis.
 - ii) **Unprovoked bite or unhealthy animal:** If the bite was unprovoked or the animal appeared unhealthy, it should be submitted for testing. If the animal is unavailable for testing, PEP should be considered.

NOTE: Birds, reptiles, amphibians, and fish do not get rabies.

RABIES FLOW CHART NOTES

1. Defined as a bite, scratch, or direct contact where there is contamination of a scratch, abrasion, mucous membrane, or open wound (one that has been bleeding in the past 24 hours) with potentially infectious material such as saliva or central nervous system tissue or fluid.
2. Contact the Massachusetts Department of Public Health (MDPH), Division of Epidemiology and Immunization for advice on human exposure. Domestic animal exposure should be reported to the local animal control official or the Massachusetts Department of Food and Agriculture (MDFA), Bureau of Animal Health. Questions about wild animal exposures and ferret exposures should be addressed to the Massachusetts Department of Fisheries and Wildlife (MDFW).
3. Wolf/hybrids are considered unvaccinated despite vaccination history.
4. The type of quarantine will be determined by the local animal inspector. Questions about all domestic animal quarantines **except ferrets** should be addressed to the Bureau of Animal Health. Questions about ferret quarantines should be addressed to the MDFW.
5. Wild rabbits are at low risk for rabies, but rabbits caged outdoors are at greater risk. Bites by wild rabbits rarely warrant prophylaxis. However, a rabbit caged outdoors that bites a human should be tested for rabies.
6. Post-exposure prophylaxis should be given in any situation where a bat is physically present and a bite, or any other exposure/contact, cannot be ruled out. In situations which there is reasonable probability that such contact occurred (e.g. a sleeping individual awakes to find a bat in the room, an adult witnesses a bat in the room with a previously unattended child, mentally challenged person, intoxicated individual, etc.), post-exposure prophylaxis is appropriate even in the absence of a demonstrable bite or scratch.
7. If a person is bitten or otherwise exposed to the saliva of a wild animal or a domesticated animal for which there is no USDA-approved rabies vaccine, the animal may need to be euthanized and tested for rabies. Since the shedding period of rabies virus in such animals is unknown, a quarantine period (e.g., of two weeks) is not appropriate in the event that a person is bitten or otherwise exposed to the animal's saliva. Contact the Massachusetts Department of Public Health (MDPH), Division of Epidemiology and Immunization for advice on human exposures to these animals. In addition, exposures to these animals should also be reported to the local animal control official or the Massachusetts Department of Food and Agriculture (MDFA), Bureau of Animal Health.

IMPORTANT TELEPHONE NUMBERS

MDPH, Division of Epidemiology and Immunization: (617) 983-6800
MDPH Virology Laboratory: (617) 983-6385, -6386, -6387
MDFW, Division of Fisheries and Wildlife: (617) 626-1591
MDFA, Bureau of Animal Health: (617) 626-1794

APPENDIX 3: RABIES POST-EXPOSURE PROPHYLAXIS SCHEDULE

If NOT PREVIOUSLY VACCINATED

Treatment	Regimen ¹
Local Wound Cleaning	All post-exposure treatment should begin with immediate, thorough cleaning of all wounds with soap and water.
Human Rabies Immune Globulin (HRIG)	20 IU/kg body weight given once on day 0. If anatomically feasible, the full dose should be infiltrated around the wound(s), the rest should be administered IM in the gluteal area. HRIG should not be administered in the same syringe , or into the same anatomical site as vaccine, or more than 7 days after the initiation of vaccine. Because HRIG may partially suppress active production of antibody, no more than the recommended dose should be given.
Vaccine	Human Diploid Cell Vaccine (HDCV), Rabies Vaccine Adsorbed (RVA), or Purified Chick Embryo Cell Vaccine (PCEC) 1.0 ml IM (deltoid area²) , one each on days 0, 3, 7, 14, and 28.

If PREVIOUSLY VACCINATED³

Treatment	Regimen ¹
Local Wound Cleaning	All post exposure treatment should begin with immediate, thorough cleaning of all wounds with soap and water.
HRIG	HRIG should not be administered
Vaccine	HDCV ,RVA or PCEC, 1.0 ml IM (deltoid area²) , one each on days 0 and 3.

CORRECT VACCINE ADMINISTRATION SITES

Age Group	Administration Site
Children and Adults	DELTOID ² only (NEVER in gluteus)
Infants and Young Children	Outer aspect of thigh (anterolateral thigh) may be used (NEVER in gluteus)

1 These regimens are applicable for all age groups, including children.

2 The **deltoid** area is the **only** acceptable site of vaccination for adults and older children. For infants and young children, the outer aspect of the thigh (anterolateral thigh) may be used. Vaccine should **NEVER** be administered in the gluteal area.

3 Any person with a history of pre exposure vaccination with HDCV, RVA, PCEC; prior post exposure prophylaxis with HDCV, RVA, PCEC; or previous vaccination with any other type of rabies vaccine and a documented history of antibody response to the prior vaccination.

APPENDIX 4: RABIES PRE-EXPOSURE PROPHYLAXIS GUIDE

Risk category	Nature of risk	Typical Populations	Pre-exposure Recommendations
Continuous	Virus present continuously, often in high concentrations. Aerosol, mucous membrane, bite or non-bite exposure. Specific exposures may go unrecognized.	Rabies research lab worker ¹ , rabies biologics production workers.	Primary course. Serologic testing every 6 months; booster vaccination when antibody level falls below acceptable level. ²
Frequent	Exposure usually episodic, with source recognized, but exposure may also be unrecognized. Aerosol, mucous membrane, bite, or non-bite exposure.	Rabies diagnostic lab workers ¹ , spelunkers, veterinarians and staff, and animal-control and wildlife workers in rabies endemic areas. Travelers visiting foreign areas of endemic rabies for more than 30 days.	Primary course. Serologic testing or booster vaccination every 2 years. ²
Infrequent (greater than population at large)	Exposure nearly always episodic with source recognized. Mucous membrane, bite, or non-bite exposure	Veterinarians and animal-control and wildlife workers in areas of low rabies endemicity. Veterinary students.	Primary course; no serologic testing or booster vaccination.
Rare (population at large)	Exposures always episodic. Mucous membrane, or bite with source unrecognized.	U.S. population at large, including persons in rabies endemic areas.	No vaccination necessary.

- 1 Judgment of relative risk and extra monitoring of vaccination status of laboratory workers is the responsibility of the laboratory supervisor.
- 2 Minimum acceptable antibody level is complete virus neutralization at a 1:5 serum dilution by RFFIT. Booster dose should be administered if the titer falls below this level.

RABIES PRE-EXPOSURE PROPHYLAXIS SCHEDULE

Type of Vaccination	Route	Regimen
Primary	IM	HDCV, RVA, PCEC, 1.0 ml (deltoid area), One each on days 0, 7, and 21 or 28
Booster ¹	IM	HDCV, RVA, PCEC, 1.0 ml (deltoid area), day 0 only

¹Administration of routine booster dose of vaccine depends on exposure risk category as noted in the table above. (Adapted from: CDC. MMWR 1999; No. RR-1.)

APPENDIX 5: RABIES – HUMAN DISEASE

A. THE AGENT

Rabies is caused by the rabies virus, a rhabdovirus which is relatively fragile, easily inactivated with disinfectants, and has a short half-life in the environment.

B. PATHOGENESIS

When a person is infected, the virus is inoculated and replicates in muscle. After a period of time, it enters the peripheral nervous system via neuromuscular spindles or motor end plates and then enters the CNS, usually via spinal cord axons. After this, there is selective and sequential infection of the limbic system, reticular formation, pontine tegmentum and cranial nerve nuclei in the floor of the fourth ventricle, inspiratory motor neurons of the nucleus ambiguus, and the neocortex and higher brain centers. After entering CNS, the virus enters other organs, including the salivary glands, where it can be shed in saliva.

C. CLINICAL PRESENTATION

The incubation period is usually 20-60 days, but can be as short as 10 days. Fewer than 1% of human cases have an incubation period longer than six months. The incubation period depends on the site of infection. If the virus is inoculated closer to the CNS or in an area more highly innervated (e.g., hand) the incubation period is usually shorter. The incubation period also depends on the severity of exposure (dose of virus) and age (younger age = shorter incubation period). During the incubation period the patient is asymptomatic.

The prodromal phase usually lasts 2-10 days and is characterized by pain and paresthesia at the site of the bite (present in 50-80% of cases) and non-specific complaints such as malaise, anorexia, fatigue, headache, and fever. Behavioral changes may also be apparent at this time, including apprehension, anxiety, agitation, irritability, insomnia, and depression.

Following the prodromal phase, the patient enters the acute neurologic phase, characterized by many possible symptoms, including: disorientation and hallucinations; ascending or asymmetrical paralysis and nuchal stiffness; episodes of terror and excitement, hydrophobia, and/or aerophobia lasting 1-5 minutes (involuntary contractions of the diaphragm); hyperventilation, hypersalivation, and focal or generalized seizures; and respiratory and cardiac arrhythmias and hypertension. These symptoms are inevitably followed by coma and death. Other symptoms that have occurred in rabies patients include muscle fasciculations, particularly at the bite site, and priapism. The acute neurologic phase lasts between 2-21 days.

D. INFECTIOUS PERIOD

The period during which a patient is infectious probably begins 1 week before symptoms onset and lasts until death. Secretions considered potentially infectious include saliva and respiratory secretions (viral concentrations in humans with rabies are 3-4 times lower than in dogs with rabies). Human to human transmission is rare. There have been six cases documented after corneal transplant. After centuries of reports of rabies, there has been no documented person-to-person transmission.

E. DIAGNOSIS

No test is 100% sensitive for antemortem diagnosis. Serum antibody to the rabies virus is not detected until 8-10 days post onset of symptoms, and CSF antibody is not detectable until more than 7 days after serum antibody. Rising serum antibody or the presence of CSF antibody is diagnostic. The Rapid Fluorescent Focus Inhibition Test (RFFIT) for neutralizing antibodies is the most common assay.

Indicators of CNS invasion include a positive DFA on antigen in the cornea, nuchal skin (nerve endings around hair follicles) or brain tissue. Negri bodies may also be seen. Isolation of virus from saliva, tracheal aspirates, and other organs/fluids is also diagnostic.

Post mortem examination of fresh brain tissue (DFA is the standard method) is the most commonly used and reliable indicator of rabies infection. Mouse inoculation for rabies virus isolation can also be used. Amplification of virus in cell culture may be useful, particularly for monoclonal antibody analysis of the virus for strain typing.

F. HOSPITAL INFECTION CONTROL

Risk of exposure is dependent upon behavior and contact with infected respiratory or salivary secretions. Traditionally, nurses and respiratory therapists are at highest risk of exposure. Other personnel are at lower risk. There has been no known nosocomial transmission of rabies. Nevertheless, “contact” isolation and universal precautions should be followed, including use of gowns, gloves, masks, and goggles. Use of soap, water, and disinfectants will inactivate any virus in the environment.

The laboratory, pathology, and funeral home personnel should be warned about high-risk specimens, such as sputum, CSF, and biopsy specimens.

Post-exposure prophylaxis in hospitals might be recommended for: bites with penetration of skin by teeth; exposure to patient’s saliva or other potentially infectious material in direct contact with a mucous membrane or broken skin (cut, scratch, abrasion); or scalpel nicks or needle sticks if in contact with CSF, nervous tissue, ocular tissue, or internal organs.

Post-exposure prophylaxis is not indicated for contact with potentially infectious material on unknown skin or after contact with blood, stool, or unspun urine.

APPENDIX 6: EPIDEMIOLOGY OF HUMAN RABIES IN THE UNITED STATES – 1980-2001¹

CASES EXPOSED IN U.S.			
Year	State	Animal (variant) ²	Type of Exposure
1981	Oklahoma	Skunk	unknown
1983	Michigan	Bat (silver-haired)	unknown
1984	Pennsylvania	Bat (myositis)	unknown
1990	Texas	Bat (free-tailed)	Bite
1991	Georgia	Bat (silver-haired)	unknown
1991	Texas	Dog/coyote	unknown
1991	Arkansas	Bat (silver-haired)	unknown
1993	New York	Bat (silver-haired)	unknown
1993	Texas	Bat (silver-haired)	unknown
1994	California	Bat (silver-haired)	unknown
1994	W. Virginia	Bat (silver-haired)	unknown
1994	Alabama	Bat (silver-haired)	unknown
1994	Tennessee	Bat (silver-haired)	unknown
1994	Texas	Dog/coyote	unknown
1995	Washington	Bat (myositis)	unknown
1995	California	Bat (silver-haired)	unknown
1995	Connecticut	Bat (silver-haired)	unknown
1995	California	Bat (silver-haired)	unknown
1996	Kentucky	Bat (silver-haired)	unknown
1996	Montana	Bat (silver-haired)	unknown
1997	Montana	Bat (silver-haired)	unknown
1997	Washington	Bat (myositis)	unknown
1997	Texas	Bat	unknown
1997	New Jersey	Bat	contact
1998	Virginia	Bat	unknown
2000	California	Bat	unknown
2000	Georgia	Bat	contact
2000	North Dakota	Bat	bite
2000	Wisconsin	Bat	unknown
TOTAL = 29			

CASES EXPOSED ABROAD				
Year	State of Residence	Country of exposure	Animal ²	Type of Exposure
1981	Arizona	Mexico	dog	bite
1983	Massachusetts	Nigeria	dog	bite
1984	Texas	Laos	dog	unknown
1984	California	Guatemala	dog	bite
1985	Texas	Mexico	dog	unknown
1987	California	Philippines	dog	unknown
1989	Oregon	Mexico	dog	unknown
1992	California	India	dog	bite
1993	California	Mexico	dog	bite
1994	Florida	Haiti	dog	unknown
1996	Florida	Mexico	dog	bite
1996	New Hampshire	Nepal	dog	bite
2000	New York	Africa	dog	bite
2001	California	Phillipines	dog	unknown
Total = 14				

¹Through July 2001

²As documented by monoclonal antibody analysis

Appendix 7: POST-EXPOSURE PROPHYLAXIS REPORTING FORM

INITIATION OF RABIES POST -EXPOSURE PROPHYLAXIS REPORTING FORM

DEPARTMENT OF PUBLIC HEALTH
SURVEILLANCE UNIT
305 SOUTH ST. BOSTON, MA 02130

PERSONAL INFORMATION

PATIENT'S LAST NAME (print clearly below)

FIRST AND MIDDLE NAME (or initials)

OCCUPATION ☐ Vet/Vet Worker ☐ Animal Control Officer ☐ Police/Firefighter ☐ Zoo/Animal Shelter Worker
☐ Dairy/Livestock Worker ☐ Wildlife Worker ☐ Other ☐ Unknown

STREET ADDRESS TOWN OR CITY STATE ZIP CODE COUNTY

DATE OF BIRTH: ___ / ___ / ___ RACE: ☐ American Indian or Alaskan Native SEX: ☐ Male
MO DAY YR ☐ Asian or Pacific Islander ☐ Black ☐ Female
☐ White ☐ Other ☐ Unk ☐ Unk

INSURANCE: ☐ uninsured ☐ work-related accident ☐ private insurance ☐ Medicaid
☐ Medicare ☐ Medicare ± supplemental ☐ other

PROPHYLAXIS INFORMATION

Date rabies post-exposure prophylaxis initiated: ___ / ___ / ___
MO DAY YR

Which of the following products were given on the day prophylaxis was initiated (Check all that apply) ?

- ☐ rabies vaccine
☐ Human Rabies Immune Globulin (HRIG)

Has the exposed person had pre-exposure rabies prophylaxis or previous post-exposure prophylaxis in this country since 1980?

☐ yes ☐ no ☐ unknown

EXPOSURE INFORMATION

Town or City and State where exposure occurred _____ Date of exposure ___ / ___ / ___

Type of exposure (check all that apply)

Direct exposure to rabid/suspect rabid animal:

- ☐ single bite
☐ multiple bites
☐ scratch
☐ saliva contaminating open wound
☐ saliva in eye, nose, mouth
☐ skinning/dressing animal
☐ touching/petting animal
☐ other. Specify _____
☐ unknown

Indirect exposure to rabid/suspect rabid animal through
contact with pet or other animal having conflict with
rabid/suspect rabid animal:

- ☐ handling pet/animal; fresh wounds on hands
☐ handling pet/animal, no fresh wounds on hands
☐ other. Specify _____

Species of exposing animal: ☐ raccoon ☐ skunk ☐ fox ☐ woodchuck
☐ cat ☐ dog ☐ bat ☐ other. Specify _____

Is the animal available for quarantine or testing? ☐ yes ☐ no ☐ unknown

Was the animal confirmed as rabid? ☐ yes ☐ no ☐ unknown

PHYSICIAN'S NAME _____ PHONE () _____

FACILITY NAME AND ADDRESS _____

Please mail or fax to The Division of Epidemiology, Bureau of Communicable Disease Control, Massachusetts Department of Public Health, 305 South Street, Jamaica Plain, Massachusetts 02130, fax: (617) 983-6813.

Appendix 8: USEFUL RABIES CONTACT INFORMATION

**The Division of Epidemiology and Immunization,
Massachusetts Department of Public Health**
(consultation about human exposures)

Weekdays	(617) 983-6800
Evenings/weekends (emergencies)	(617) 983-6200

Rabies Laboratory Massachusetts State Laboratory Institute	(617) 983-6385, -6386, -6387
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The Bureau of Animal Health, Department of Food and Agriculture (to report domestic animal or livestock exposures and for questions regarding domestic animals or livestock)	(617) 626-1794
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The Division of Fisheries and Wildlife, Department of Fisheries, Wildlife and Environmental Law Enforcement (for questions about wild animal and ferret exposures)	(617) 626-1591
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Human Rabies Immune Globulin (HRIG)

Aventis-Pasteur (manufacturer and distributor of “Imogam”, HRIG)	1-800-VACCINE
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Human Rabies Vaccine

Chiron Corporation (manufacturer and distributor of PCEC)	1-800-CHIRON-8
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Aventis-Pasteur (manufacturer and distributor of HDCV)	1-800-VACCINE
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BioPort Corporation (licensed, but <i>not</i> currently manufacturing or distributing RVA)	(517) 327-1500
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Labs performing RFFIT on human specimens:

Atlanta Health Associates, Inc.	1- 800-717-5612
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NE Georgia Reference Laboratory	(706) 613-0077
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Maryland State Rabies Lab	(410) 767-6176
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